1. **A preventive vaccine targeting both Human papillomavirus α genotypes causing anogenital cancers and β genotypes causing non-melanoma skin cancers**

**Global Integrative Oncology: Use in Cancer Treatment & Patient Management**

Human papillomavirus (HPV) is a family of small DNA tumor viruses including over 200 genotypes classified by phylogeny into several genera. The α genus HPV genotypes generally infect the anogenital mucosa and a high-risk subset, e.g. HPV16 and HPV18, cause cervical, other ano-genital and oropharyngeal cancers. By contrast, the HPV genotypes of the β genus, e.g. HPV5, produce typically benign cutaneous infections, but can synergize with sunlight exposure and immunosuppression to cause non-melanoma skin cancer. Epidermodysplasia verruciformis (EV) patients, as well as solid organ transplant recipients and HIV+ patients are especially prone to non-melanoma skin cancer associated with βHPV. Licensed preventive vaccines are composed of virus-like particles (VLPs) derived by expression of major capsid protein L1. They confer protection generally restricted to the 9 αHPVs included in vaccine and their associated anogenital cancers and genital warts, but do not protect against βHPV. We developed a novel vaccine in which a broadly protective epitope (RG1) from the HPV minor capsid protein L2 is displayed within an immunodominant surface loop of HPV16 L1. Vaccination with this chimeric RG1-VLP vaccine induced L2 antibodies that neutralized and protected against all oncogenic αHPV types. To provide protection against βHPV we developed a second chimeric HPV18 L1 VLP displaying an RG1-like epitope better designed to target βHPVs. Here we show that vaccination of mice the combination of the two chimeric VLPs induces robust serum titers of L2-specific antibodies reactive against all βHPV genotypes tested. Importantly, these vaccinated mice were fully protected against challenge with HPV5 (a βHPV associated with skin cancers), whereas only partial protection was evident in animals vaccinated with just the original RG1-VLP designed to target αHPV. In sum, this bivalent vaccine has potential to protect against infections of both α genotypes causing anogenital cancers and β genotypes causing non-melanoma skin cancers.

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